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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,036	03/22/2006	Osamu Cynshi	CYNSHI 7	4404

1444 7590 01/13/2009

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EXAMINER	
KEYS, ROSALYND ANN	

ART UNIT	PAPER NUMBER
1621	

MAIL DATE	DELIVERY MODE
01/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,036	CYNSHI ET AL.	
	Examiner	Art Unit	
	Rosalynd Keys	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 17-34 are pending.

Claims 17-34 are rejected.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 20, 2008 has been entered.

Response to Arguments

3. Applicant's arguments filed November 20, 2008 have been fully considered but they are not persuasive.

The Applicants submit, using for support the teachings of Spaniol et al. and Quaglino et al., that one skilled in the art would not have expected from the disclosures of Tamura et al. and Tsujii et al. that the compounds of claims 17-31 are useful for the treatment of fatty liver or hepatic disease.

This submission is not persuasive because the mitochondrial toxicity of amiodarone and the B0 and B2 analogues of amiodarone appears to be due to the coupling of the benzofuran ring to the p-OH-benzene structure rather then simply the benzofuran ring. In support of this belief, the Examiner submits the following teachings:

1) Masazumi et al. (JP 05-320169), which teach a benzofuran derivative is taught to exhibit an action to inhibit the increase in the activity of ALT and is useful for the prevention and treatment of hepatopathy (see entire computer generated English translation, in particular paragraphs 0002-0010). It is also taught that the hepatopathy depressant, which is the benzofuran derivative expressed with formula (I) is safe for Homo sapiens (see paragraph 0049).

2) Royer et al. (US 3,808,236), which teach that the compounds 3, 5, 6-trimethyl-2-nitro-benzofuran (R 4906) and 2-nitro-benzofuran (R 5144) can be used in therapy for the treatment of hepatic amoebiasis (see column 2, lines 38 and 39; column 6, lines 14 and 15; and column 9, lines 9-12). Hepatic amoebiasis is a well known infection of the liver with a single-celled parasite called Entamoeba histolytica.

3) Ookawa et al. (JP 1-213276), which teach a benzofuran derivative which is useful for treatment or prophylaxis of dysfunction of heart, brain, lung, kidney or liver (see attached Derwent abstract).

4) Cynshi et al. (US 6,133,279), which teach a compound having the claimed formula for use as a preservative for the liver (see entire disclosure, in particular column 5, line 65 to column 7, line 29; column 15, lines 18-28; and Tables 1 and 2 in columns 33 and 34).

Based upon the teachings of Masazumi et al., Royer et al., Ookawa et al. and Cynshi et al. the skilled artisan would reasonably believe that the benzofuran ring is not the cause of the mitochondrial toxicity of amiodarone and the B0 and B2 analogues of amiodarone. Thus, based upon the teachings of Tamura et al. in view of Tsujii et al. the

compounds of claims 17-31 would be expected to be useful for the treatment of fatty liver or hepatic disease.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 17-34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tamura et al (US 5,574,178) in view of Tsujii et al (US 5,043,354).

The instant claimed invention is directed to the use of compounds of formula 1 (shown in clam 1) to treat fatty liver or hepatic diseases.

Tamura et al teach a genus which embraces the compounds used in the instant claims (see columns 1-10). Tamura discloses that the compounds have antioxidant properties and are useful for treating arteriosclerosis, myocardial infarction and other ischemia diseases (see column 1, lines 9-46 and column 2, line 54 to column 3, line 23).

Tamura fails to explicitly teach that the compounds could be useful for treating fatty liver or hepatic diseases.

Tsujii discloses benzofuran compounds that are useful in the treatment of diseases causes by reactive oxygen species (see column 1, lines 9-12), which means that these compounds are antioxidants. Tsujii list ischemic diseases and myocardial infarction as typical diseases that can be treated with the benzofuran compounds (see column 1, lines 35-46). Tsujii also listed disorders of the liver as diseases that would be treatable using the benzofuran antioxidants. Thus Tsujii establishes that ischemia, myocardial infarction and disorders of the liver are treated by the same method.

It would have been obvious to one having ordinary skill in the art at the time that applicant's invention was made to have used the compounds of Tamura to treat disorders of the liver, as taught by Tsujii. Fatty liver and hepatic diseases are subgeneric to the phrase disorders of the liver. Thus a skilled artisan would have had a

reasonable expectation of success in using the compounds in Tamura in the treatment of fatty liver and hepatic diseases including aspartate aminotransferase leaking from the liver cells into the blood. One skilled in the art would have been motivated to use the compounds in Tamura to treat other diseases which are affected by the same mechanism. ***"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solution, a person of ordinary skill in the art has good reason to pursue the know options within his or her technical grasp" (SUPREME COURT OF THE UNITED STA TESS, KSR INTERNATIONAL CO. v. TELEFLEX INC. et al, April 30, 2007; 550 U.S. 2007)***.

8. Claims 17-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cynshi et al. (US 6,133,279) in view of Ookawa et al. (JP 01213276A).

Cynshi et al. teach a compound having the claimed formula (1) for use as an antioxidant which inhibits against lipid peroxidation (see entire disclosure, in particular column 1, line 5 to column 2, line 67; column 5, line 65 to column 7, line 29; column 15, lines 18-28; and Tables 1 and 2 in columns 33 and 34). Cynshi et al. (US 6,133,279) teach that the compounds having the claimed formula 1 are useful as a preservative for the liver (see column 15, lines 18-28).

Although Cynshi et al. teach the compounds having the claimed formula 1 are useful as a preservative for the liver, they do not expressly teach the use of the compounds having the claimed formula 1 for the treatment of fatty liver or hepatic diseases, which include aspartate aminotransferase leaking from the liver cells into the blood.

Ookawa et al. (JP 1-213276) teach a benzofuran derivative of the formula (I), which is useful for treatment or prophylaxis of dysfunction of heart, brain, lung, kidney or liver (see attached Derwent abstract). It is further taught that since (I) inhibits lipid peroxidation, 5-lipoxygenase, thromboxane A2 synthetase or oxygen-derived free radical generation, they can be used for treatment of prophylaxis of thrombosis, ischaemic disease (e.g., myocardial infarction, cerebral apoplexy), nephritis, lung insufficiency, asthma, psoriasis vulgaris, inflammation, immediate allergy, atherosclerosis, fatty liver, hepatitis, liver cirrhosis, immunodeficiency, tumours, etc.

It would have been obvious to one having ordinary skill in the art at the time that applicant's invention was made to have used the compounds of Cynshi et al. to treat liver or hepatic diseases, such as those taught by Ookawa et al., since like the compounds of Ookawa et al., the compounds of Cynshi et al. are antioxidants which inhibit lipid peroxidation. Thus a skilled artisan would have had a reasonable expectation of success in using the compounds in Cynshi et al. in the treatment of fatty liver and hepatic diseases including aspartate aminotransferase leaking from the liver cells into the blood. One skilled in the art would have been motivated to use the compounds in Cynshi et al. to treat other diseases which are affected by the inhibition of lipid peroxidation. ***"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solution, a person of ordinary skill in the art has good reason to pursue the know options within his or her technical grasp" (SUPREME COURT OF THE UNITED STA TESS, KSR INTERNATIONAL CO. v. TELEFLEX INC. et al, April 30, 2007; 550 U.S. 2007)***.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosalynd Keys whose telephone number is (571)272-0639. The examiner can normally be reached on M & T 5:30 am-7 am & 9:30 am-4:30 pm: W-F 8:00 am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rosalynd Keys/
Primary Examiner, Art Unit 1621

January 8, 2009